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EXAMINER	
KIM, YOUNG J	

ART UNIT	PAPER NUMBER
1637	

NOTIFICATION DATE	DELIVERY MODE
03/03/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/588,631	DENOMME, GREGORY A.	
	Examiner	Art Unit	
	Young J. Kim	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 January 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-37* is/are pending in the application.

4a) Of the above claim(s) *3-36* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 and 37* is/are rejected.

7)☒ Claim(s) *1 and 2* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *07 August 2006* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/7/06 & 4/28/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I, consisting of claims 1, 2, and 6 and SEQ ID Numbers 3 and 4 in the reply filed on January 15, 2009 is acknowledged.

It appears that Applicants' election of the single primer set is drawn to an oligonucleotide set which is for detecting RHDe92 and RHDe9A, and thus claim 6, directed to an oligonucleotide set for HPA-1 detection is withdrawn from further consideration as being drawn to non-elected invention.

The traversal is on the ground(s) that the primers and probes disclosed in the application do not encode protein or polypeptide per se but enable the detection of single nucleotide polymorphisms (SNPs) in blood group and/or platelet antigen and thus the search should not be unduly burden to the Office (page 7, Response). This is not found persuasive because Applicants' arguments drawn to "search burden" is not applicable under National phase. In addition, each of the oligonucleotides is directed to different mutations found on different genes, which are clearly different in their sequences, and thus lacking in sharing of a special technical feature.

Applicants' submission of new claim 37 is hereby rejoined because the method requires the elected set of primers, and thus are joined herein for prosecution. Applicants are advised that should Applicants' further add limitations to claim 37 or submit dependent claims which require additional probe sequences, the amended/new dependent claims will be withdrawn as being drawn to non-elected invention (election occurring by original presentation), as Group III clearly sets forth that a method requiring a combination of probes and primers are drawn to different inventions.

The requirement is still deemed proper and is therefore made FINAL.

Claims 4-25 and 30-36 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on January 15, 2009.

Preliminary Remark

Claims 1, 2, and 37 are pending are under prosecution herein.

Priority

The priority date accorded is February 6, 2004, based on provisional application – 60/541,932 - which supports the subject matter under prosecution.

Information Disclosure Statement

The IDS received on August 7, 2006 and April 28, 2008 are proper and are being considered by the Examiner.

Drawings

New corrected drawings in compliance with 37 CFR 1.121(d) are required in this application because figures 1 and 4 are too small to be legible. Applicant is advised to employ the services of a competent patent draftsperson outside the Office, as the U.S. Patent and Trademark Office no longer prepares new drawings. The corrected drawings are required in reply to the Office action to avoid abandonment of the application. The requirement for corrected drawings will not be held in abeyance.

Claim Objections

Claims 1 and 2 are objected to for being drawn to non-elected invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 37 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 37 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: a pair of oligonucleotides which are capable of amplifying RHCE gene.

Claim 37 is examined solely based on it being drawn to the detection of RHD, exon 9, via use of primer pairs consisting of SEQ ID Numbers 3 and 4.

Applicants' recitation of "RHD***/RHCE***" wherein the underlined embodiment appears to be a typographical error as the **primer pairs is capable of amplifying exon 9 of RHD**, and ***not exon 9 of RHCE*** (see page 20 of the amended specification). Removing the underlined embodiment from both the preamble and the step of the claim would overcome this rejection.

In addition, the pair of SEQ ID Numbers 3 and 4 appear to be specific for identifying ***A/G*** single nucleotide polymorphism (see page 26, Table 1, showing a pair of RHDe9S and RHDe9A primers amplifying RHD exon 9, with SNP "A/G"), but the claim recites that the SNP detected is G/A. For the purpose of prosecution, the mutation disclosed in the specification is assumed.

Applicants' are requested for clarification.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 37 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a New Matter Rejection.

Claim 37 is a newly added claim, and thus does not constitute application as originally filed.

Claim 37 recites that the primer pair of SEQ ID Number 3 and 4 allow the detection of SNP in an RHD gene, wherein the SNP is G/A.

However, the instant specification is clear that the pair of SEQ ID Numbers 3 and 4 is specific for identifying ***A/G*** single nucleotide polymorphism (see page 26, Table 1, showing a pair of RHDe9S and RHDe9A primers amplifying RHD exon 9, with SNP "A/G").

Thus, the present claim introduces new matter.

Removal of new matter is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Flegel et al. (WO 99/37763 A2, published July 29, 1999).

Flegel et al. disclose a nucleic acid sequence comprising 100% identity to SEQ ID Number 4 (see below):

```
SEQ ID NO: 4

  Query Match             100.0%;  Score 24;  DB 1;  Length 1254;
  Best Local Similarity   100.0%;  Pred. No. 2.5;
  Matches   24;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 TTGGTCATCAAAATATTTAGCCTC 24
              ||||||||||||||||||||||||
Db       1215 TTGGTCATCAAAATATTTAGCCTC 1192
```

Since a product is solely defined by its physical element and its intended use is not given patentable weight, the claim has been construed a nucleic acid comprising the sequence depicted in Table 1.

As noted above, the nucleic acid disclosed by Flegel et al. clearly comprises the nucleic acid of SEQ ID Number 4 and thus anticipate the invention as claimed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 2, and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hyland et al. (U.S. Patent No. 5,972,602, issued October 26, 1999), Lee et al. (Database accession number ss1530464; SNP (NCBI) [Online], September 13, 2000; IDS ref), and Okuda et al. (Biochemical and

Biophyscial Research Communications, 2000, vol. 274, pages 670-683) as evidenced by Maaskant-van Wijk (herein, "Wijk"; Transfusion, December 1998, vol. 38, pages 1015-1021; IDS ref).

Hyland et al. disclose that the rhesus blood group antigens are clinically important because of their highly immunogenic nature (column 1, lines 22-23) and that five most commonly typed Rh antigens are C/c, E/e and the D antigen which is the most immunogenic (column 1, lines 31-32).

Hyland et al. disclose that the past practices typed RhD by performing agglutination with human polyclonal anti-D sera, to the progression of typing agglutination with IgM and/or blends of IgM and IgG anti-D monoclonal antibodies, but notes that these methods were not robust as the antibodies, "may not detect some weak RhD antigens and RhD variants" (column 1, lines 42-47).

Hyland et al. disclose a method of typing RhD by PCR amplification (column 4, lines 62-67), noting the advantage of such a practice:

> "There are a number of advantages with RhD genotyping by this PCR method. Firstly, PCR using DNA enables the RhD genotype of an individual to be unambiguously known…Other applications of RhD PCR genotyping exists in Rh paternity testing and in family and genetic studies using Rh as an inheritance marker ... Secondly, ... RhD PCR method does not require red blood cells or large quantities of human tissues ..." (column 7, lines 25-36; Hyland et al.)

Hyland et al. do not employ the primer pair of SEQ ID Numbers 3 and 4 which amplify a specific single nucleotide polymorphism A/G in exon 9 of RHD gene.

Lee et al. disclose that A/G SNP found on exon 9 of the RHD gene was known and available to the public prior to the filing date (as early as September 13, 2000) of the instant application.

Okuda et al. evidences that the entire gene sequence of RHD was known and available:

> "We determined the entire nucleotide sequences of all introns within the RHD and RHCE genes by amplifying genomic DNA using long PCR methods. The RHD and RHCE genes were 57,295 and 57,831 bp in length, respectively" (page 670, 1st column; Okuda et al.)

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to arrive at the pair of oligonucleotide primers of SEQ ID Numbers 3 and 4 for amplifying a known single nucleotide polymorphism from RHD – a gene whose sequence was entirely known (as evidenced by Okuda et al.) for the following reasons.

Hyland et al. clearly evidences the useful nature of genotyping RHD gene for clinical studies (see above), as well as the advantage of employing a PCR reaction for such typing (see above).

While Hyland et al. are not explicit in stating that exon 9 of the RHD gene should have been typed, one of ordinary skill in the art would have understood that gene markers such as known SNPs would have been useful for clinical genotyping.

Such importance was already expressed by Hyland et al. (as discussed above) as well as Okuda et al., wherein Okuda et al. expresse:

> "The Rh blood group discovered by Levine and Stetson (1) is clinically ***one of the most important blood groups***." (page 670, 2nd column, 1st paragraph; Okuda et al.)

Thus, one of ordinary skill in the art at the time the invention was made would have been clearly motivated to employ known markers such as those disclosed by Lee et al. for genotyping RHD gene.

Provided that the entire gene sequences was known and that Lee et al. already disclosed the SNP found on RHD gene, one of ordinary skill in the art would have been clearly able to derive a primer which flank the known SNP, as such would have involved empirical determination of trial and error.

In *KSR International Co. v. Teleflex Inc. (KSR)*, 550 U.S. __, 82 USPQ2d 1385 (2007), the Supreme Court particularly emphasized "the need for caution in granting a patent based on the combination of elements found in the prior art," *Id.* at __, 82 USPQ2d at 1395. The Supreme Court

further expressed that, "[t]he combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results." *Id.* at __, 82 USPQ2d at 1395.

Such is the case here. The claims are drawn to a primer pair which flanks a known single nucleotide polymorphism. Since the motivation to genotype RHD gene for clinical purposes, and as the target nucleic acid (RHD gene) was entirely known and available to the public, as well as the location of the mutation, one of ordinary skill in the art would have been clearly capable of deriving at any primer pairs, such as that which is claimed in the application, as such would have involved routine experimentation of trial and error.

Lastly, claims 1 and 2 are drawn to a product, wherein the elected invention is only directed to a single primer pair consisting of SEQ ID Numbers 3 and 4 (and claim 37 toward its method of use). However, even if one were to argue that the primer sequence of SEQ ID Numbers 3 and 4 were designed for multiplex analysis, the motivation to genotype RHD by multiplex PCR was already evidenced by Wijk. And designing of primers for multiplex amplification only involves trial and error of different primer sequences, the determination of which would be within the purview of an ordinarily skilled artisan.

Therefore, the invention as claimed is deemed *prima facie* obvious over the cited artisans.

Conclusion

No claims are allowed.

Inquiries

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Young J. Kim whose telephone number is (571) 272-0785. The Examiner is on flex-time schedule and can best be reached from 9:00 a.m. to 5:30 p.m (M-F). The Examiner can

also be reached via e-mail to Young.Kim@uspto.gov. However, the office cannot guarantee security through the e-mail system nor should official papers be transmitted through this route.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Gary Benzion, can be reached at (571) 272-0782.

Papers related to this application may be submitted to Art Unit 1637 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant does submit a paper by FAX, the original copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office. All official documents must be sent to the Official Tech Center Fax number: (571) 273-8300. For Unofficial documents, faxes can be sent directly to the Examiner at (571) 273-0785. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Young J. Kim/
Primary Examiner
Art Unit 1637
2/27/2009

/YJK/